REMARKS

The present invention is directed to methods of treatment for specific non-albicans species of *Candida* isolates using antimycotic delivery systems. These systems are suitable for use in the vaginal cavity. The invention is additionally concerned with methods utilizing preparations demonstrating a controlled, extended or sustained release of the active and/or therapeutic agent and a minimal number of administrations to produce efficacy upon administration of said delivery system.

Upon entry of the forgoing amendments, claims 1-27 are pending in the application. Claims 1, 17 and 22 have been amended to clarify the language contained therein. The amendments do not add any new matter within the meaning of 35 U.S.C. §132. Accordingly, entry of the amendments to the claims as noted above is respectfully requested.

In view of the following, further and favorable consideration is respectfully requested.

REJECTION UNDER 35 U.S.C. §102(b):

Claims 9 and 24-27 stand rejected under 35 U.S.C.§102(b) as being anticipated by Brown, et al., *Journal of Reproductive Medicine*, in view of Stedman's Medical Dictionary ("Brown" and "Stedman's", respectively).

Applicants respectfully traverse this rejection, and request reconsideration and withdrawal thereof.

The test for anticipation is whether each and every element as set forth is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of California,* 2 USPQ2d 1051, 1053 (Fed. Cir. 1987); MPEP § 2131. The identical invention must be shown in as complete detail as is contained in the claim. R*ichardson v. Suzuki Motor Co.,* 9 USPQ2d 1913, 1920 (Fed. Cir. 1989); MPEP §2131. The elements must also be arranged as required by the claim. *In re Bond,* 15 USPQ2d 1566 (Fed. Cir. 1990).

Claim 9 is directed to a method for the treatment of an unidentified vulvovaginal fungal condition, which comprises: administration to said fungal condition a bioadhesive, single dose treatment formulation comprising from about 0.500 to about 5.000% w/w butoconazole nitrate; and wherein the unidentified vulvovaginal fungal condition is caused by a *Candida* species selected from the group consisting of *dubliniensis*, *tropicalis*, *glabrata*, *parapsilosis*, *krusei*, and *lusitaniae*.

Claim 24 is directed to a method for the treatment of an unidentified vulvovaginatis condition comprising: treating a condition caused by a species of *Candida* selected from the group

consisting of *C. dubliniensis*, *C. tropicalis*, *C. glabrata*, *C. parapsilosis*, *C. krusei*, and *C. lusitaniae* by applying to the vaginal tissue a multiphase formulation in a single dose to provide a *Candida* species kill rate of about 50 to about 100% for a period of at least about 4 days. Claims 25-27 all depend, from claim 24.

In contrast to the presently claimed subject matter, Brown is directed to a comparison of the safety and efficacy of a single vaginal dose of butoconazole nitrate 2% sustained release cream with a seven day schedule of miconazole nitrate 2% vaginal cream in the treatment of vulvovaginal candidias caused by *C. albicans*. See, Objective, Introduction, Patient Selection, and Results: Microbiological Cure Rate sections. Steadman's simply provides a definition for "cream" as meaning a semisolid emulsion of either the oil-in-water type, ordinarily intended for topical use.

Applicants submit that Brown in view of Stedman's does not teach each and every element of the claims 9 or 24-27 as required for anticipation under 35 U.S.C. § 102(b). Specifically, Brown in view of Stedman's does not teach administration of a bioadhesive single dose treatment formulation comprising from about 0.500 to about 5.000% w/w butoconazole nitrate to a **vulvovaginal fungal condition caused by a *Candida* species selected from the group consisting of *dubliniensis*, *tropicalis*, *glabrata*, *parapsilosis*, *krusei*, and *lusitaniae*** as recited in claim 9. Additionally, Brown in view of Stedman's does not teach treating a **condition caused by a species of *Candida* selected from the group consisting of *C. dubliniensis*, *C. tropicalis*, *C. glabrata*, *C. parapsilosis*, *C. krusei*, and *C. lusitaniae*** by applying to the vaginal tissue a multiphase formulation in a single dose to provide a *Candida* species kill rate of about 50 to about 100% for a period of at least about 4 days as recited in claim 24.

Although Brown teaches that vulvovaginal Candidiasis is **caused by *C. albicans*** as well as non-albicans pathogenic species, Brown only teaches that the single-dose butoconazole is **effective in treating *C. albicans*, alone**. *See* Brown at page 934 and page 936, second paragraph. According to Brown et al., "[a]bsence of *C. albicans* in fungal cultures constituted the microbiological cure." *Id.* Accordingly, it is clear that Brown et al. only contemplates the treatment of *C. albicans*. In view of the teaching that the cured condition Brown is represented by the absence of *C. albicans* in fungal culture, the mere teaching that there are 150 known species of *Candida*, only 9 of which are pathogens, is certainly not sufficient to establish the Examiners assertion that Brown teaches treating a condition caused by a *Candida* species selected from the group consisting of *dubliniensis*, *tropicalis*, *glabrata*, *parapsilosis*, *krusei*, and *lusitaniae* as recited in claims 9 and 24. **Treatment of pathogens other than C. albicans is not addressed in Brown.**

Accordingly, Applicants submit Brown in view of Steadman's does not teach each and every element of claims 9 and 24-27, as required for anticipation under 35 USC § 102(b). Therefore, Applicants respectfully request that the Examiner reconsider and withdraw this rejection.

REJECTION UNDER 35 U.S.C. §103(a):

Claims 1-27 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Riley in U.S. Patent No. 5,266,329 (the '329 patent), in view of Brown, *supra*, and Garg in *Pharmaceutical Tech. Drug Delivery* ("Garg"), and Droegemueller et al. in *Obstet. Gynecol* ("Droegemueller").

Applicants respectfully traverse the rejection of claims 1-27 under 35 U.S.C. §103(a). A *prima facie* case of obviousness has not been established with respect to the '329 patent, in view of Brown and Garg and Droegemueller for the reasons set forth below.

Applicants respectfully traverse this rejection because *prima facie* case of obviousness has not been established.

To establish a *prima facie* case of obviousness, the Examiner must establish: (1) some suggestion or motivation to modify the references exists; (2) a reasonable expectation of success; and (3) the prior art references teach or suggest all of the claim limitations. *Amgen, Inc. v. Chugai Pharm. Co.*, 18 USPQ2d 1016, 1023 (Fed. Cir. 1991); *In re Fine*, 5 USPQ2d 1596, 1598 (Fed. Cir. 1988); *In re Wilson*, 165 USPQ 494, 496 (CCPA 1970).

It is submitted that a *prima facie* case of obviousness has not been established because nothing in any of the applied references, taken alone or together, teach or suggest all of the limitations of the claims as required by *In re Wilson*.

All of independent claims 1-35 are, generally, directed to the use of a bioadherant, single dose **treatment** of a vulvovaginitis condition **caused by** non-albicans species of *Candida*. Specifically, claims 1-35 are directed to treating conditions caused by *Candida* species including: *dubliniensis*, *tropicalis*, *glabrata*, *parapsilosis*, *krusei*, and *lusitaniae*.

In contrast, the '329 patent teaches systems and methods of preparation and administration thereof, which release an active agent in a controlled manner for an extended period in a vaginal cavity environment. The disclosure teaches that when the system incorporates an antifungal agent, i.e., an imidazole, the

conventional treatment time may be reduced by at least 25%. Specifically, the '329 patent teaches that the conventional treatment period or quantity of agent used is reduced by at least 25%, whereas normally a controlled release drug system reduces the number of times a day that a drug must be administered rather than the overall length of treatment. See, col. 4, lines 5-20. **The '329 patent teaches that tests utilizing imidazoles upon *C. albicans*** have demonstrated this result. The '329 patent does not teach or suggest the use of a bioadherent, single-dose treatment of a vulvovaginatis condition caused by non-albicans as presently claimed.

Brown does not remedy the deficiencies of the '329 patent. Brown is discussed above with regard to the rejection under 35 U.S.C. § 102(b). Brown does not teach or suggest the use of a bioadherent, single-dose treatment of a vulvovaginatis condition caused by non-albicans as presently claimed. Therefore, whether taken alone, or in combination, the '329 patent and Brown do not render the presently claimed subject matter obvious.

Garg does not remedy the deficiencies of the '329 patent and Brown. Garg is directed to pharmaceutical excipients useful in vaginal formulations. Garg does not teach or suggest the use of a bioadherent, single-dose treatment of a vulvovaginatis condition caused by non-albicans as presently claimed. Therefore, whether taken alone, or in combination, the '329 patent, Brown and Garg do not render the presently claimed subject matter obvious.

Droegemueller does not remedy the deficiencies of the '329 patent, Brown and Garg. Droegemueller is directed to a three day treatment with butoconazole nitrate for vulvovaginal candidiasis. The teachings of Droegemuller are limited to *C. albicans*.

Accordingly, Droegemueller does not teach or suggest the use of a bioadherent, single-dose treatment of a vulvovaginatis condition caused by non-albicans as presently claimed. Therefore, whether taken alone, or in combination, the '329 patent, Brown, Garg, Droegemueller do not render the presently claimed subject matter obvious as all of the elements are not taught or suggested as required to establish a prima facie case of obviousness under 35 U.S.C. § 103(a).

In view of the foregoing, it is submitted nothing in the '329 patent, Brown, Garg, Droegemueller, taken alone or in combination, renders the presently claimed subject matter obvious within the meaning of 35 U.S.C. § 103(a). Applicant respectfully submits a prima facie case for obviousness has not been established. Accordingly, the Examiner is respectfully requested to withdraw this rejection.

CONCLUSION

In view of the foregoing, Applicants submit the pending claims are in condition for allowance. Early notice to this effect is earnestly solicited. The Examiner is invited to contact the undersigned attorney if it is believed such contact will expedite the prosecution of the application.

If the Examiner has any questions or comments regarding this matter, he is welcomed to contact the undersigned attorney at the below-listed number and address.

Respectfully submitted,

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